Proton Beam Therapy at UCLH

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## Cancer Types & Survival Rates


### Five-year relative survival

- **Women**
  - Testis: 95%
  - Hodgkin’s lymphoma: 84%
  - Melanoma: 78%
  - Bladder: 71%
  - Larynx: 67%
  - Prostate: 61%
  - NHL: 51%
  - Colon: 46%
  - Rectum: 45%
  - Kidney: 45%
  - Leukaemia: 45%
  - Multiple myeloma: 22%
  - Ovary: 34%
  - Leukaemia: 36%
  - Kidney: 43%
  - Colon: 45%
  - Rectum: 48%
  - NHL: 52%
  - Bladder: 61%
  - Cervix: 68%
  - Uterus: 76%
  - Breast: 79%
  - Hodgkin’s lymphoma: 83%
  - Melanoma: 90%
  - Pancreas: 3%
  - Lung: 3%
  - Oesophagus: 5%
  - Uterus: 76%
  - Brain: 12%
  - Breast: 13%
  - Multiple myeloma: 24%
  - Leukaemia: 38%
  - Kidney: 45%
  - Rectum: 45%
  - Colon: 46%
  - NHL: 51%
  - Prostate: 61%
  - Larynx: 67%
  - Bladder: 71%
  - Leukaemia: 36%

- **Men**
  - Testis: 95%
  - Hodgkin’s lymphoma: 84%
  - Melanoma: 78%
  - Bladder: 71%
  - Larynx: 67%
  - Prostate: 61%
  - NHL: 51%
  - Colon: 46%
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  - Larynx: 67%
  - Bladder: 71%
  - Leukaemia: 36%

### Survival Rates

- **10-50% survival:**
  - 29% of cases diagnosed

- **More than 50% survival:**
  - 38% of cases diagnosed

- **Less than 10% survival:**
  - 24% of cases diagnosed
The Bragg Peak

\[- \frac{dE}{dx} = \frac{4\pi}{m_e c^2 \beta^2} n z^2 \left( \frac{e^2}{4\pi \epsilon_0} \right)^2 \left[ \ln \left( \frac{2m_e c^2 \beta^2}{I (1 - \beta^2)} \right) - \beta^2 \right] \]

**Bethe-Bloch:**

- $E$ = energy
- $x$ = distance
- $m_e$ = electron mass
- $n$ = electron density
- $z$ = particle charge
- $\beta$ = particle velocity
- $e$ = electron charge
- $\epsilon_0$ = vacuum permittivity
- $I$ = mean excitation potential
60 MeV Bragg Peak in Liquid Scintillator
Protons Vs. Photons: Medulloblastoma
Protons Vs. Photons: NSC Lung Cancer

Fig. 1. A typical case comparison between IMRT and IMPT. (a) Dose distributions for the IMRT (left) and IMPT (right) plans are shown. Each line delineates the PTV. (b) DVHs are shown for the IMRT plan (squares) and IMPT plan (triangles). Ips., ipsilateral; Con., contralateral.

Protons Vs. Photons: NSC Lung Cancer

Zhang X, Li Y, Pan X, et al.
Int J Radiat Oncol Biol Phys.
2009;77(2):357-366

(19.8% mean absolute improvement in V5, 27% mean absolute improvement in contralateral lung V5), heart (14.2% mean absolute improvement in heart V40), esophagus (6.8% mean absolute improvement in esophageal V55), and spinal cord (9.5 Gy mean absolute improvement in spinal cord maximal dose) than IMRT did (Table 1).

More importantly, IMPT allowed radiation dose escalation from 63 Gy up to 83.5 Gy, with a mean MTD of 74 Gy in this study.

Fig. 2. Comparison between IMRT and IMPT MTD. (A) Dose distributions for the IMRT plan at 63 Gy (left) and IMPT MTD plan at the MTD of 80 Gy (right). Each line delineates the PTV. Of note is that the esophagus was overlapped by the CTV and PTV for this patient, whereas the IMPT MTD plan was able to reduce the esophageal dose to less than 80 Gy. (B) DVHs for the IMRT plan (squares) and IMPT MTD plan (triangles). Ips., ipsilateral; Con., contralateral.

Reduced dose and individualized radical RT by IMPT

X. ZHANG et al. 361

IMRT PBT

Anatoly Bugorski

- Researcher at the Institute for High Energy Physics in Protvino, working on U-70 synchrotron.
- On 13 July 1978, safety mechanisms failed while Bugorski was checking some malfunctioning equipment when he stuck his head in the path of the proton beam.
- He saw a flash “brighter than a thousand suns,” but did not feel any pain.
- The left half of Bugorski’s face swelled up and started peeling off over the next several days, revealing the proton beam path.
- Despite receiving a dose believed to be far in excess of fatal, Bugorski survived and even completed his PhD.
- There was virtually no damage to his intellectual capacity, but the fatigue of mental work increased markedly.
- The left half of his face was paralysed; he completely lost hearing in his left ear.
- He was able to function well, except for the fact that he had occasional complex partial seizures and rare tonic-clonic seizures.
Accelerators and Gantries

- Use a particle accelerator to get the beam up to 250 MeV.
- Delivered to patient through gantry.
- Gantry must be big enough to deliver beam from any angle: 3 stories tall!
- UCLH and The Christie will each have 3 gantries.
Pencil beam scanning allows better conformal dose to be delivered to target volume.

- Beam delivered in small “pencil” beams and scanned across target.
- Energy modulated by accelerator: target subdivided into layers and “painted” by using energy variation.
UK Proton Therapy

• Currently UK only has 1 proton therapy centre: Clatterbridge (Wirral) treats eyes with 60 MeV protons.
• Around 20 existing proton therapy centres worldwide with around the same number planned.
• Most countries treat private patients with simple tumours (85% prostate…).
• Some British children sent abroad for treatment in Jacksonville, FL.
• Earlier this year, government gave the go ahead for 2 new cancer treatment facilities using protons:
  – UCLH.
  – Manchester/Christie.
• Procurement began 2013, up and running in 5 years.

UK Proton Therapy Indications

- Indications list is available on the web:
- Will treat most difficult cases:
  - Brain: Chordoma, Glioma, Craniopharyngioma, Meningioma, Intracranial Germinoma.
  - Skeletal: Chondrosarcoma, Rhabdomyosarcoma, Osteosarcoma, Ewings sarcoma.
  - Central Nervous System: Ependymoma, Medulloblastoma (PNET), Spinal Sarcoma.
  - Head & Neck: Retinoblastoma, Nasopharynx, Acoustic Neuroma, Choroidal Melanoma.
  - Others: Hodgkins.

### Table: List of Indications for UK Patients

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric</td>
<td></td>
</tr>
<tr>
<td>Chordoma/Chondrosacoma</td>
<td>15</td>
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<tr>
<td>Rhabdomyosarcoma (Orbit)</td>
<td>5</td>
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<tr>
<td>Rhabdomyosarcoma (Prameningeal and H&amp;N)</td>
<td>15</td>
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<tr>
<td>Rhabdomyosarcoma (Pelvis)</td>
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<tr>
<td>Osteosarcoma</td>
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<tr>
<td>Ewings</td>
<td>9</td>
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<tr>
<td>PPNET</td>
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<tr>
<td>Ependymoma</td>
<td>25</td>
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<tr>
<td>Low Grade Glioma</td>
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<tr>
<td>Optic Pathway Glioma</td>
<td>12</td>
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<tr>
<td>Cranipharyngioma</td>
<td>15</td>
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<tr>
<td>Medulloblastoma (PNET)</td>
<td>70</td>
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<tr>
<td>Hodgkins</td>
<td>5</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>5</td>
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<tr>
<td>Meningioma</td>
<td>3</td>
</tr>
<tr>
<td>Intracranial germinoma</td>
<td>10</td>
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<tr>
<td>Nasopharynx (H&amp;N)</td>
<td>15</td>
</tr>
<tr>
<td>Difficult Cases Esthe/Neuro/Liver)</td>
<td>5</td>
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<tr>
<td>Very Young Age</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>252</td>
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<tr>
<td>Adult</td>
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<tr>
<td>Choroidal Melanoma</td>
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<td>Ocular/Orbital</td>
<td>25</td>
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<tr>
<td>Chordoma</td>
<td>60</td>
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<tr>
<td>Chondrosarcoma</td>
<td>30</td>
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<tr>
<td>Para-Spinal/Spinal Sarcoma</td>
<td>120</td>
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<tr>
<td>Sacral Chordoma</td>
<td>60</td>
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<tr>
<td>Meningoma</td>
<td>100</td>
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<tr>
<td>Acoustic Neuroma</td>
<td>100</td>
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<tr>
<td>Craniospinal NOS (Pineal)</td>
<td>10</td>
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<tr>
<td>Head &amp; Neck &amp; Paranasal Sinuses</td>
<td>300</td>
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<tr>
<td>PNET (medulloblastoma Intracranial)</td>
<td>30</td>
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<tr>
<td>Difficult cases</td>
<td>300</td>
</tr>
<tr>
<td>Total</td>
<td>1,235</td>
</tr>
<tr>
<td>GRAND TOTAL</td>
<td>1,487</td>
</tr>
</tbody>
</table>
UCLH Cancer Campus

1. 250 EUSTON ROAD
2. UCHL MAIN WING
3. MAPLE HOUSE
4. MAPLE HOUSE LABORATORIES
5. UCHL EGA WING
6. ROSENHEIM BUILDING
7. ODEON SITE
8. ROCKEFELLER BUILDING
9. PAUL O'GORMAN BUILDING
10. CANCER CENTRE
11. HOSPITAL FOR TROPICAL DISEASES
12. 70 HUNLEY STREET
13. 62 HUNLEY STREET
14. ROYAL EAR HOSPITAL
15. CHENIES MEWS
16. 46-60 HUNLEY STREET
17. MAPLE HOUSE FLATS
18. PAUL'S HOUSE (CLIC SARGENT)
19. PROPOSED PATIENTS' HOTEL
20. 170 TOTTENHAM COURT ROAD
21. WHITFIELD STREET LABORATORIES
22. BONHAM CARTER HOUSE / WARWICKSHIRE HOUSE

Simon Jolly, UCL
UCLH Proton Therapy Site

- New facility will be on existing UCLH site, next to Tottenham Court Road.
- Linked to UCLH via walkways to allow easy patient transfer.
- Planning to treat ~750 patients a year.
- 1 proton accelerator feeding 3/4 gantries (plus research room).
- Total cost: £150 million.
Down Comes The Rosenheim...
Down Comes The Rosenheim…

Simon Jolly, UCL
Down Comes The Rosenheim...
Down Comes The Rosenheim...
UCLH PBT Cut-through (Old)
Censored
Censored
Censored
Key Areas for Research

- Imaging.
- Adaptive Therapy.
- Imaging.
- Patient Throughput.
- Imaging.
- Pathways (Data Management).
- Imaging.
- Dose Verification.
- Imaging.
- Charged Particle Dosimetry.
- Imaging.
- Neutron Dosimetry.
- Imaging.
- Variable Spot Size.
- Imaging.
- Compact Gantry.
- Imaging.
- Radiobiology
Range Uncertainty

- The advantage of protons is that they stop.
- The disadvantage is that we don’t always know where...
- Range verification:
  - in vivo, direct (e.g. PET, prompt), indirect (e.g. calibrated CT, other decoupled method).
  - Calibrate with phantom.
- Proton radiography/tomography:
  - e.g. PRaVDA: Si detector range telescope with tracker at entrance and exit.
  - becoming a big area internationally; underdeveloped but not complex.
  - Working on better calorimetry for proton CT at UCL.
Proton Dose with Tumour Motion

Heng Li, PhD
Department of Radiation Physics
UT MD Anderson Cancer Center
(Yoshikazu Tsunashima)
• Imaging is **WITHOUT QUESTION** the most important challenge for proton therapy.
• High resolution imaging required for treatment planning.
• Imaging required between fractions to monitor changes in patient anatomy/tumour volume.
• In an ideal world:
  – Real-time imaging DURING TREATMENT to EXACTLY where internal anatomy is relative to nozzle.
  – Coupled to instantaneous measurement of radiobiological damage (not just dose!) during beam delivery.
  – This gives you information on precisely where dose is being delivered and whether it’s being delivered in the right place…
• Clinicians will ask you for this many times over before even thinking about the accelerator…
• Proton CT goes some way towards this (better resolution than X-ray CT) but will need multi-modality imaging.
• Adaptive Therapy seeks to modify treatment on-the-fly: lots of work already under way.

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Dose Verification

• Need to optimise “patient scheduling” and “beam scheduling” to maximise throughput:
  – Patient treatment timetable planned a week or so in advance: how do you arrange treatments to treat as many patients each day?
  – Beam scheduling based on patient scheduling, but must be highly reactive:
    • Redirect beam if patient not ready, needs to be realigned, problems with GA etc.
    • Need to optimise beam availability, minimise switching and tuning time.

• Could be the difference between 3 rooms and 4…
Other Requirements

• Data Management:
  – Patients will be referred to UCLH/Christie from across UK.
  – Large range of referring centres, each with their own patient database: patient notes, imaging etc.
  – Will need:
    • Streamlined and transparent patient referral system (particular issue for personalised treatments)
    • Engagement of referring centres: boundary of responsibility/planning between referring hospital and treatment centres.
  – Massive amounts of data needs to be centralised:
    • Information collated at PBT centres to inform treatment.
    • Post treatment planning information passed back to original referring centre.

• Dosimetry:
  – Any particle that is not a proton at the correct energy needs to be monitored and minimised.
  – Need species and energy spectra of charged particles, photons and neutrons.

• Dose Verification:
  – Relative dose verification already established: verify dose distribution from given treatment plan.
  – Need ABSOLUTE dose as well: how many protons per spot?
  – Work being led by NPL.

• Variable Spot Size:
  – Larger beam spots have more overlap than small spots.
  – Good for making dose more uniform in centre of tumour, bad for reducing hard edge of treatment volume.
  – Variable spot size would allow dynamic change in all 3 dimensions to get best possible compromise of overlap and conformality.

• Compact Gantries: smaller = cheaper = better…
• At the moment, virtually all innovation in proton therapy is coming from the research sector (just not in the UK…).
• Commercial manufacturers will ALWAYS follow the money (for sound financial reasons):
  – No commercial carbon solutions.
  – No proton CT systems.
  – No fast beam switching.
  – No “novel” accelerator solutions.
  – Lots of work integrating existing solutions: in-room X-ray CT, multi-leaf collimators, robotic couches etc.
• So if you want to develop new technology, it needs to be reasonably mature before you can interest any of the commercial partners!
• Building it yourself is another option: anybody have a spare £250m…?
• Also need to address the question of clinical approval: this never comes as quickly as you’d hope (see Mevion, ProTom).
• Innovation sorely lacking in the UK in this area: will need significant public investment before we can get to a stage of commercial viability.
• STFC, it’s over to you…
Acknowledgements

• My thanks to the following people for providing me with information (most of it without their knowledge...):

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  – Ran Mackay
• Manchester:
  – Hywel Owen
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